



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Richard T. Dean et al.

Art Unit : 1654

Serial No. : 08/236,402

Examiner : Jeffrey Russel

Filed : May 2, 1994

Title : TECHNETIUM-99M LABELED IMAGING AGENTS

RECEIVED

JUL 29 2003

DECLARATION UNDER 37 C.F.R. § 1.132

TECH CENTER 1600/2900

I, RICHARD T. DEAN, declare as follows:

1. I reside in Newmarket, New Hampshire.
2. At the time that this application was filed, I was President and Chief Executive Officer of Diatech, Inc. (which subsequently changed its name to Diatide, Inc.), the Assignee of the above-identified patent application.
3. I have a Ph.D. in Chemistry from the University of California, Berkeley, and extensive knowledge of all aspects of radiolabelling of proteins and peptides, particularly radiolabelling with technetium 99m.
4. I am one of the named inventors in this application and, in April of 1990, I conceived of the concept of modifying the carboxy terminus or the N-terminus of peptides for labelling with technetium 99m in the manner set forth in this patent application.

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

24 JULY 2003

Date of Deposit

Signature

*Maryann White*

MARYANN WHITE

Typed or Printed Name of Person Signing Certificate

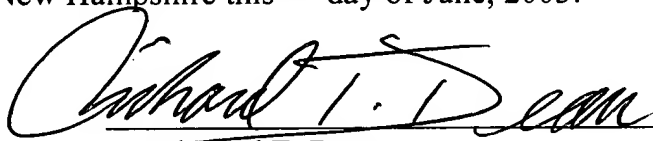
Applicant : Richard T. DEAN et al.  
Serial No. : 08/236,402  
Filed : May 2, 1994  
Page : 2 of 2

Attorney's Pocket No.: 09744-006001 / DITI 107

5. Attached hereto are copies of the front page and pages 1, 2, 3, 4, 161 and 162 of my notebook RTD 1. Pages 1-4 were signed by me on 11 April 1990. Pages 161 and 162 were signed by me on 16 September 1991.

I declare further that all statements made here of my own knowledge are true that all statements on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Signed at Newmarket, New Hampshire this <sup>24</sup> day of June, 2003.

  
Richard T. Dean

RTD-1

THIS BOOK BELONGS TO

Richard T. Dean

Diatech Inc.

~~CLASS OF~~ \_\_\_\_\_

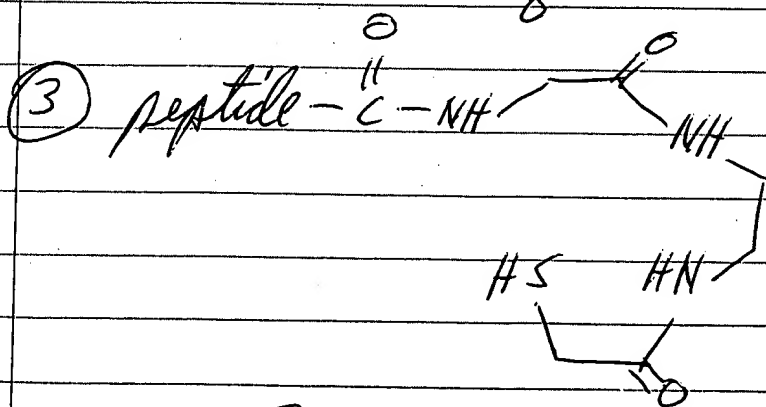
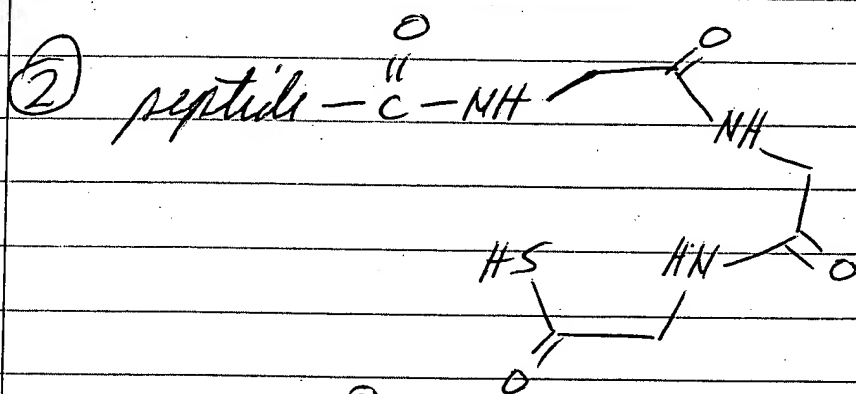
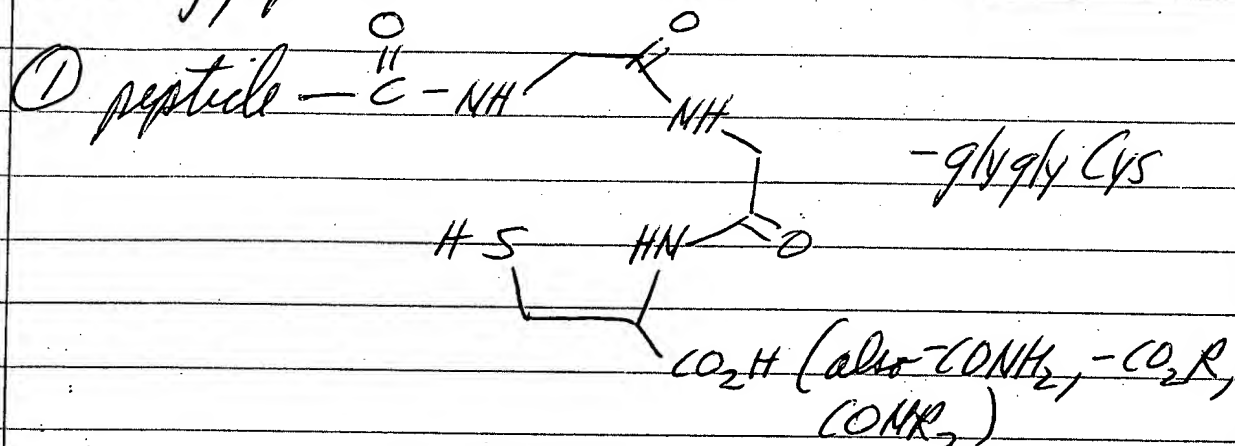
April 11, 1990

A record of research ideas  
and research work performed for  
Diatech Inc.

HARVARD COOPERATIVE SOCIETY  
CAMBRIDGE, MASS.

# Compositions for Modifying the Carboxy Terminus of A Peptide for Labeling with Technetium-99m

The following compositions are proposed for labeling peptides with Technetium-99m;

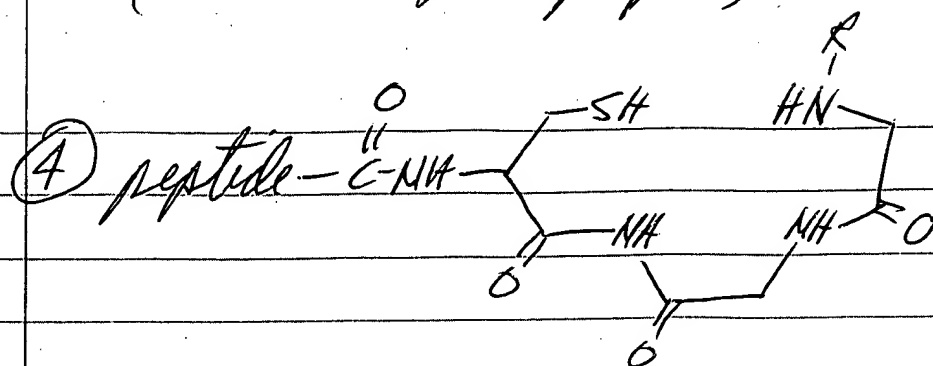


Richard T. Dean 4/11/90

Read & understood by: N. L. L. L.

date: 4/11/90.

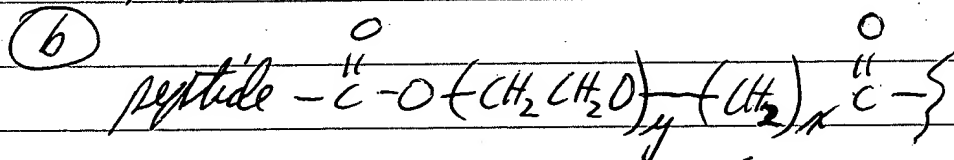
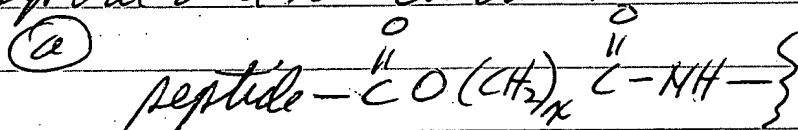
(continued from page 1)



where R can be H, acyl or alkyl

(-Cys Gly Gly)

⑤ ester linked spacers between the peptide and the chelate:



where x and y are small integers

⑥  $\text{peptide}-\text{CO}-\text{Ser Ser Cys}$

⑦  $\text{peptide}-\text{CO}-\text{Cys Ser Ser}$

⑧  $\text{peptide}-\text{CO}-\text{Tyr Gly Cys}$

Richard T. Dean

4/11/90

Read and understood by: A. Lumber

Date: 4/12/90

# Compositions for Modifying the N-Terminus of Peptides for Labeling with Technetium-99m

The following compositions are proposed for labeling peptides with Tc-99m:

- (1)  $\text{HSCH}_2\overset{\text{O}}{\underset{\text{||}}{\text{C}}}\text{NH-peptide}$
- (2)  $\text{HSCH}_2\overset{\text{O}}{\underset{\text{||}}{\text{C}}}\text{NH-Gly Gly Gly-peptide}$
- (3)  $\text{HSCH}_2\overset{\text{O}}{\underset{\text{||}}{\text{C}}}\text{NH-Ser Ser Ser-peptide}$
- (4)  $\text{Cys Gly Gly-CO NH-peptide}$
- (5)  $\text{Cys Gly Gly Gly-CO NH-peptide}$

Richard T. Dean

4/11/90

Read + understood by: Mudi Kumbale Date: 4/20/90

# Compositions for Imaging with Technetium-99m

The following peptides are proposed for labeling with Tc-99m and imaging.

- (1) RGDGGC, RGDGGGC
- (2) RGDSGGC, RGDSGGGC
- (3) CGGRGD, CGGGRGD
- (4) CGGRGDS, CGGGRGDS
- (5) mercaptoacetyl-GGGRGD  
mercaptoacetyl-GGGRGDS
- (6) mercaptoacetyl-GGRGD  
mercaptoacetyl-GGGRGDRGD
- (7) mercaptoacetyl-GGG-NH- $\begin{cases} \text{CO-RGD(S)} \\ (\text{CH}_2)_x \text{CO-RGD(S)} \end{cases}$

where  $x = 0-6$

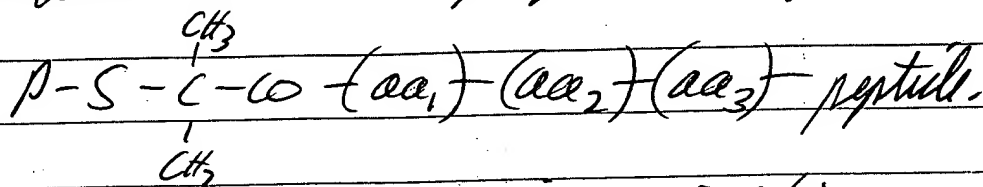
Richard I. Dean

4/11/90

Read + understood by: Anthea Lammle Date: 4/20/90

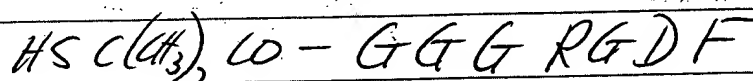
9/16/91 Peptides with a Group for Labeling with Tc-99m

An  $N_3S$  system for labeling peptides with Tc-99m is proposed as follows:



Where  $aa$  is any amino acid (i.e.  $\alpha$  amino acid) and each may be the same or different,  $P$  is either H or a suitable protecting group.

A non-limiting example is:



Richard T. D. Dan

9/16/91

Witnessed by: Scott, Sullivan 16 Sept 91



9/16/91 Tc-99m Labeled Peptides

Peptides which have a C-terminal sequence as follows are useful for labeling with Tc-99m:

peptide  $(aa_1)(aa_2)-Pen$

Where  $(aa)$  is any  $\alpha$ -amino acid, Pen is penicillamine and the peptide is a peptide with a specific binding region.

Chillard Tc-99m

9/16/91  
Witnessed by: Scott Subram 16 Sept 91